Impact of the Diabetes Canada Guideline Dissemination Strategy on the Prescription of Vascular Protective Medications: A Retrospective Cohort Study, 2010-2015

Alanna V Rigobon[1], MSc, Sumeet Kalia[2], MSc, Jennica Nichols[3,4], MSc, Babak Aliarzadeh[2], MD MPH, Michelle Greiver[2,6,7], MD MSc, Rahim Moineddin[2], PhD, Frank Sullivan[2,5,6,7], MB, ChB(Hons) PhD, Catherine Yu[8], MD MHSc.

[1] Faculty of Medicine, University of Toronto
[2]University of Toronto Practice Based Research Network, Department of Family & Community Medicine
[3]Diabetes Canada
[4] Interdisciplinary Studies, University of British Columbia
[5] Medical School, University of St Andrews, Scotland
[6]North York General Hospital, [7]Institute for Clinical Evaluative Sciences (ICES)
[8]Department of Medicine, Division of Endocrinology & Metabolism, University of Toronto

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Address for correspondence:

Catherine Yu

St. Michael's Hospital

61 Queen Street East, Room 7-034

Toronto, ON, M5C 2T2

ABSTRACT

Objectives: The 2013 Diabetes Canada guidelines launched targeted dissemination tools and a simple assessment for vascular protection. We aimed to: (1) examine changes in the rates of vascular protective medications prescribed in primary care for older patients with diabetes associated with the launch of the 2013 guidelines, and (2) examine differences in the rates of vascular protective prescriptions by patient and provider characteristics.

Research Design and Methods: The study population included patients (≥40y) from the Canadian Primary Care Sentinel Surveillance Network (CPCSSN) with type 2 diabetes and at least one clinic visit from April 2010-December 2015. An interrupted time-series (ITS) analysis was used to assess the proportion of eligible patients prescribed an HMG-CoA Reductase Inhibitor (statin), ACE-Inhibitor (ACEI)/Angiotensin Receptor Blocker (ARB), or antiplatelet prescription in each quarter. Proton Pump Inhibitor (PPI) prescriptions were the reference control.

Results: A dynamic cohort was used where participants were enrolled each quarter using a pre-specified set of conditions (range 25,985-70,693 per quarter). There were no significant changes in statin (p=0.43), ACEI/ARB (p=0.42), antiplatelet (p=0.39) or PPI (p=0.16) prescriptions at baseline (guideline intervention). After guideline publication, there was a significant change in slope for statins (-0.52%/quarter; standard error [SE] 0.15, p<0.05), ACEI/ARBs (-0.38%/quarter; SE 0.13, p<0.05) and reference PPI prescriptions (-0.18%/quarter; SE 0.05, p<0.05).

Conclusions: There was a decrease in prescribing trends over time that was not specific to vascular protective medications. More effective knowledge translation strategies are needed to improve vascular protection in diabetes in order for patients to receive the most effective interventions.

INTRODUCTION

The World Health Organization (WHO) describes the 'rule of halves' whereby half of the people with long-term conditions are not known, half of those known are not treated and half of those treated are not controlled (1). As a result of these failures patients with diabetes are at increased risk of developing significant morbidity and mortality related to atherosclerotic cardiovascular complications including coronary heart disease, stroke and peripheral vascular disease (2). The lifetime 10-year cardiovascular disease (CVD) risk is >20% for patients aged >40 years and living with diabetes (3). Effective risk factor modification with vascular protective medications, including statins, antihypertensive agents and antiplatelet agents is an essential component of diabetes management to improve both quantity and quality of life years (3,4). Clinical trial data show a 22-37% risk reduction in CVD for patients age >40 years on statin therapy, and a 25% risk reduction for patients age >55 years taking ACE inhibitors (ACEIs) (4–6). Despite evidence-based support for these therapies, a national physician survey in 2012 estimated that 43% of patients with diabetes do not meet guideline-recommended LDL targets (≤2 mmol/L) and 64% fail to meet BP targets (<130/80 mmHg), suggesting suboptimal vascular protection management (7).

To bridge this evidence to practice gap for vascular protection in patients with diabetes, dissemination tools were launched with the 2013 Diabetes Canada (previously Canadian Diabetes Association) evidence-based guidelines. Compared with previous (2008) guidelines, the 2013 Diabetes Canada guidelines no longer require providers to stratify patients into different risk categories prior to recommending vascular protective therapy, thereby simplifying the assessment for vascular protection (Supplemental Table 1). Statin use is recommended for all

patients ≥40 years and living with diabetes; ACEIs or angiotensin receptor blockers (ARBs) are recommended for patients ≥55 years with diabetes. Antiplatelet medications are no longer recommended for routine use in the primary prevention of CVD for patients with diabetes (3). Diabetes Canada also expanded on their patient- and provider-directed dissemination and implementation strategy, which was based on the Knowledge-to-Action Cycle and included a variety of new dissemination tools (8). The nation-wide disemination strategy launched in April 2013 and targeted multiple national and provincial systems-level groups (e.g. government agencies, non-governmental agencies, disease advocacy groups, and professional associations), as well as health care providers and people living with diabetes across Canada via large scale communications campaigns (e.g. television, radio, digital and print media) (Supplemental Table 2) (9). Interventions including in-person lecture series, conferences, webinars, web-based professional and patient resources such as flowsheets, electronic point of care decision support, a mobile application, and Electronic Medical Record (EMR) templates were rolled out over 24 months. An evaluation of the effectiveness of this dissemination strategy has been published elsewhere (9).

Multiple studies examining vascular protective agents in Canada have shown an increase in statins and ACEIs/ARBs prescribed and used over the past two decades (10–12). Estimates from one Canadian province (Ontario) suggest that statin prescriptions in patients with diabetes aged >65 years have increased 53% from 1996-2010 and ACEI/ARB prescriptions have increased by 22% over a 6-year period (1995-2001) (11,12). These studies used data from provincial drug registries, which failed to capture non-prescription medications including antiplatelets and typically involved smaller geographic areas (i.e. city or provincial level data), making it difficult

to determine if dissemination and implementation of the Diabetes Canada guidelines achieved a population-level impact across Canada. Drug registry data also exclude the population of patients with diabetes age <65 years who may be eligible for vascular protective therapy. In addition, there are no studies that examined the prescription of these medications before and after the 2013 Diabetes Canada guidelines were released and disseminated, leaving the impact of the guidelines unknown.

Successful guideline evaluation is critical in assessing whether suggested recommendations have been adopted into practice at a population level. The current study used data from the Canadian Primary Care Sentinel Surveillance Network (CPCSSN), a pan-Canadian EMR surveillance system, to capture longitudinal trends in vascular protective agent prescriptions. The specific aims were to: (1) examine changes in the rates of vascular protective medications prescribed in primary care for older patients with diabetes associated with the launch of the 2013 Diabetes Canada Guidelines and additional dissemination efforts, and (2) examine differences in the rates of vascular protective medication prescriptions according to provider and patient characteristics.

RESEARCH DESIGN AND METHODS

Study Design and Population

We used a retrospective cohort design and followed the STROBE guidelines (13). We included patients living with diabetes whose data were in the CPCSSN database from April 2010 to December 2015. Diabetes was defined according to the CPCSSN validated case definition (Supplemental Table 3) (14). The study cohort was dynamic, and patients were enrolled quarterly when the following three temporal conditions were met: [1] Onset of diabetes recorded

in the EMR prior to or during each quarter of interest, [2] First patient visit recorded within a given quarter or any quarter preceding it, [3] Patient met eligibility criteria for the medication being analyzed defined as per the 2013 Diabetes Canada guideline criteria: patients age ≥40 years for statins; age ≥55 for ACEI/ARBs. For antiplatelet agents, patients age ≥40 years with no cardiovascular event were included as guideline changes suggest that these medications should no longer be used for primary prevention in this group. Priorities set were based on well-accepted guideline recommendations and framed such that in our defined cohorts, those prescribed the agent are "controlled", and those not prescribed the agent are "uncontrolled". Achievement of LDL targets (≤2 mmol/L) and blood pressure (BP) targets (<130/80 mmHg) were assessed in patients in the following age categories: age ≥40 years for LDL, age ≥55 years for BP. We employed a censoring point whereby patients were removed from the cohort using the last encounter date if they had not seen their family doctor as indicated by an encounter in the EMR in the last two years. The study was approved by the University of Toronto's Research Ethics Board (REB#33127).

CPCSSN Database

CPCSSN, established in 2008, is an EMR-based information system designed for chronic disease surveillance. Every three months, EMR data from primary care practices in 10 practice-based research networks (PBRNs) across Canada are extracted, cleaned and merged into a single database housed at the Centre for Advanced Computing at Queen's University in Kingston, Ontario (15). Contributing PBRNs are located in Alberta (2), British Columbia (1), Manitoba (1), Newfoundland and Labrador (1), Nova Scotia (1), Ontario (3) and Quebec (1). The network is composed of over 1,100 family physicians contributing data for more than 1,500,000 patients.

Information contained in the database includes network and provider identifiers, de-identified patient demographic information, date and type of each patient's encounters, patient health conditions, risk factors, referrals, laboratory investigations, procedures and medications (15). CPCSSN captures all medications recorded in the EMR, including medications prescribed by primary care providers or specialists, and those purchased over the counter.

Data Collection and Processing

Data from January 1st 2010 to December 31st 2015 were used for this project. The project data included patient demographic variables (year and month of birth, sex, and neighbourhood level socioeconomic status (SES) indicators derived from residential postal codes), physical measurements (height, weight, body mass index (BMI), systolic BP, diastolic BP), diabetes-related laboratory records (i.e. total cholesterol, LDL, HDL, triglycerides, urine albumin/creatinine ratio), comorbidities/risk factors (i.e. hypertension, CVD, dyslipidemia, microalbuminuria, smoking history), all medications prescribed to patients (i.e. lipid lowering agents, ACEIs, ARBs, antiplatelets, and PPIs as a reference control), and provider/site characteristics (i.e. province of site, rurality of site) for each quarter of interest, and CPCSSN patient and provider data table (containing information on hierarchical relationship between patient, care provider, site and network). Year of medical school graduation for providers was collected from the University of Toronto PBRN (UTOPIAN) network only due to limited availability at other PBRNs.

All medications in CPCSSN database were coded using Anatomical Therapeutic Chemical (ATC) codes; these codes were used to identify the relevant medications for this project (16).

Long-term conditions were identified using CPCSSN validated algorithms where available (i.e. diabetes mellitus and hypertension; Supplemental Table 3). For the rest of conditions we used coded and free text diagnosis data from CPCSSN health conditions table; this table populates data from Cumulative Patient Profile (CPP) (14). CVD was defined according to guideline and antiplatelet indications to include ICD-9 codes for coronary heart disease (410-414), cerebrovascular disease (430-438), and peripheral vascular disease (440-445) (17). Dyslipidemia was defined using appropriate medication history, coded and free text diagnosis data, and included patients on lipid-lowering therapy or with LDL >2.0 mmol/L. Albuminuria was defined according to Diabetes Canada guidelines, whereby a urine albumin creatinine ratio <2 mg/mmol was normal, 2-20 mg/mmol was considered microalbuminuria, and >20 mg/mmol was macroalbuminuria (18). SES, was measured in accordance with the Canadian Institute for Health Information method of deriving neighbourhood-level deprivation indices on a quintile scale for each patient (19). Rurality was defined according to postal code whereby a second letter of "0" was considered rural and a second letter "1 to 9" considered urban (20). In accordance with recommendations of the WHO and Health Canada, BMI was classified as underweight (<18.5 kg/m^2), normal weight (18.5–24.99 kg/m^2), overweight (25–29.99 kg/m^2), obese class I (30–34.99 kg/m^2), obese class II (35–39.99 kg/m^2) and class III (≥40 kg/m^2) categories (21).

Analysis

This study used an interrupted time-series (ITS) design. For the primary analysis, the proportion of eligible patients who had prescriptions for statins, ACEI/ARBs and antiplatelets in each quarter was computed using a longitudinal data analysis (22). Quarterly intervals were chosen to introduce less fluctuation in the time-series curve compared to a monthly approach (23). If

patients had multiple visits within a quarter, the most recent record was used for all variables studied. A total of 8 quarters before, 1 quarter during, and 9 quarters after the intervention were analyzed. Patients were deemed to be prescribed a statin, ACEI/ARB or antiplatelet agent if they had any prescription record in the four preceding quarters and one quarter after each quarter of interest (lag4, lead1) (Figure 2). This approach was used to account for variation in refill protocols and prescription procedures among family physicians (i.e. some provide a prescription every three months, others provide multiple repeats) (24). Having 4 quarters before and 1 after each quarter of interest would provide a sufficient timeframe to capture prescriptions given on a yearly basis. We also examined other approaches, including (lag0, lead0), (lag1, lead1), (lag2, lead2), (lag3, lead3), (lag4, lead4), and (lag4, lead1). We found that prescription rates for the latter three approaches were very similar, further justifying our selection of the lag4, lead1 approach.

The Diabetes Canada guidelines and dissemination strategy launched April 2013, was considered the intervention point (2013Q2). A segmented regression model was used to assess baseline trend/slope, the level change immediately after intervention, and the trend/gradual change (25). We also measured the prescription rates of statin, ACEI/ARB and antiplatelets using a cross-sectional study design, which deemed a patient to be using the medication if they had at least one prescription during the entire study period (2010Q1-2015Q4). This approach serves as a sensitivity analysis for the lag4, lead1 approach and allowed us to test for subgroup differences in the proportion prescribed statin, ACEI/ARB and antiplatelets.

Secondary analyses included the proportion of eligible patients attaining LDL (≤2.0 mmol/L) or

BP targets (<130/80 mmHg). A carryover approach was implemented: each patient's most recent measurement was used in the following quarters until a new measurement was recorded in the EMR. A segmented regression model was used to assess the baseline trend/slope, level change and trend/gradual change for secondary outcomes (i.e. eligible patients attaining LDL or BP targets).

Results were stratified by patient characteristics (age, sex, BMI, SES), presence of risk factors/comorbidities (smoking, CVD, hypertension, dyslipidemia, albuminuria) and provider characteristics (province of care, rurality). We assessed the statistical significance across patient, provider and geographical characteristics for prescription rates for statins, ACEI/ARBs and antiplatelet agents using chi-square test (adjusted for multiple hypothesis testing). We used the method of false discovery rate to control for inflated Type I error rates in multiple hypothesis testing procedure (26). PPI prescriptions were used as a reference to control for confounding factors. Using modified hypothesis testing, we compared the temporal difference in prescription rates of PPIs to all three vascular protective medications (e.g. statin 2011Q2-2015Q3 vs PPI 2011Q2-2015Q3), and considered statistical significance at $p<0.05$. The analyses were conducted using SAS v.9.4 (27).

RESULTS

Primary Outcomes

The total number of patients enrolled in each dynamic cohort is outlined in Table 1. Quarterly cohort size ranged from 23,016-70,693 patients (Supplemental Table 4).. Variation in population size was attributed to increasing recruitment of practices into the CPCSSN database over time.

Results of the ITS analysis are presented in Table 2 and graphically in Figure 1. There were no significant changes in the rate of statin, ACEI/ARB, antiplatelet or PPI prescriptions prior to the release of the 2013 guidelines. After guideline publication, there was a significant change in slope for statins (-0.52%/quarter; standard error [SE] 0.15, $p<0.05$) and ACEI/ARBs (-0.38%/quarter; SE 0.13, $p<0.05$) prescribed. A significant change in slope was also seen for PPI prescriptions (-0.18%/quarter; SE 0.05, $p<0.05$). The change in slope was not significant for antiplatelets. The absolute difference in the rates of statin, ACEI/ARB, or antiplatelet prescriptions from the start (2011 Q2) to the end (2015 Q4) of the study period were significantly less than that of the PPI reference control ($p<0.0001$).

Geographic Characteristics

Prescription rates in eligible patients were significantly higher in urban compared to rural practices for statins, ACEI/ARBs, and antiplatelets across the study period (Table 2(a)-(c)). Chi-square test revealed significant differences in prescriptions rates between provinces for statins ($p<0.001$), ACEI/ARBs ($p<0.001$), and antiplatelets ($p<0.001$). Statin and ACEI/ARB prescription rates were highest in the province of Quebec (74.2% for statins; 55.9% for ACEI/ARBs) and the Maritimes (64.8% for stains; 50.5% for ACEI/ARBs) and lowest in Alberta (45.1% for statins; 39.5% ACEI/ARBs) and British Columbia (35.2% for statins; 41.5% ACEI/ARBs).

Provider Characteristics

There were no significant differences between MD graduation groups for statin ($p=0.152$) or ACEI/ARB ($p=0.18$) prescriptions in the UTOPIAN population (Table 2 (a)-(c)). However, there

were significant differences between MD graduation groups for antiplatelet prescriptions ($p<0.001$). Antiplatelet prescription rates were 20.9% for MD graduation years of 1965-1979, 15.3% for 1980-1994, and 18.3% for ≥1995.

Patient Demographics and Risk Factors

Prescription rates according to patient characteristics are seen in Table 2(a)-(c). There were no significant gender-based differences in prescription rates for statins ($p=0.99$), ACEI/ARBs ($p=0.71$) or antiplatelet agents ($p=0.15$). Patients with hypertension had significantly higher statin ($p<0.001$), ACEI/ARB ($p<0.001$), and antiplatelet ($p<0.001$) prescription rates compared to patients without hypertension. Patients with CVD also had higher statin ($p<0.001$) and ACEI/ARB ($p<0.001$) prescription rates compared to patients without CVD. Patients without dyslipidemia had significantly lower rates of statin prescription ($p<0.001$), ACEI/ARB prescriptions ($p<0.001$), and antiplatelet prescriptions ($p<0.001$) compared to those with dyslipidemia. Significant differences were detected for age groups, SES quintiles, smoking status, hypertension, dyslipidemia, and albuminuria for all three vascular protective medications ($p<0.05$). Significant differences between BMI groups were seen with respect to ACEI/ARB prescriptions ($p<0.001$).

Secondary Outcomes

LDL and BP Targets

Across the study period, LDL and BP targets were achieved by 47-57% and 61-66% of patients, respectively (Figures 1(b)-(c)). The release of the 2013 guidelines did not significantly impact the proportion of patients achieving BP targets as there were no significant changes in this

proportion before, during or after guideline release (Table 1). The release of the guidelines did not impact the proportion of patients achieving LDL targets, as there were no significant changes in this proportion during or after guideline release.

CONCLUSIONS

The results of this large study suggest that dissemination of the 2013 Diabetes Canada guidelines was not associated with any further improvements in physician prescribing behaviour as measured by EMR prescription estimates for primary vascular protection in patients age ≥40 years with diabetes. While there was no change in prescriptions at the intervention point, a small but statistically significant decrease in slope after guideline publication was observed with statins and ACEI/ARBs, as well as the reference control. A negative change in slope (improved guideline adherence) was also observed with antiplatelets, however this change was not significant. There were no significant changes with respect to LDL and BP targets at or after guideline intervention. Overall prescription rates were influenced by factors including rurality, province, and patient age and SES. While statistically significant changes were seen across patient/provider characteristics, these do not necessarily represent clinical significance given the large sample size.

Our time-series analysis revealed a negative change in slope for statins, ACEI/ARBs and PPIs. Due to a lack of sufficient variation in the time-series curves shown in Figure 1(a)-(c), the reader is cautioned that this statistical inference can be affected by minuscule change in prescription rates during any quarter pre- and post-guideline implementation (28). This decrease was also seen with the PPI comparator suggesting that external factors cannot be excluded. It is possible

that there was no actual improvement in vascular protective prescribing after release of the 2013 guidelines. The CPCSSN population also involves a dynamic cohort, so a change in composition of patients, physicians or sites included in the database in each quarter could also influence prescription rates. Entry to the dynamic cohort was random, and there would be no reason to suspect that patients with diabetes from practices joining CPCSSN later would be more likely to have lower prescribing rates. We also did not observe any remarkable shifts with respect to composition of site locations, but did observe an increase in patients age 40-49 from 5.89% to 9.15% across the study period. Patients in this age category had lower statin and ACEI/ARB prescription rates, and thus an increase in the proportion of these patients may have contributed to the measurable decrease seen in prescribing rates over time. It is also possible that an emerging focus on resource stewardship in medical education and practice, influenced physicians to prescribe more cautiously, decreasing prescription rates over time (29).

Our prescription estimates are lower than those from 2003 and 2008 Diabetes Canada guideline evaluations (7,30). These studies used physician self-reported survey data, subject to selection bias as physicians willing to participate may be those that prescribe in accordance with guideline recommendations. A validation study is currently ongoing to compare our results with data from the Institute for Clinical and Evaluative Sciences, (ICES), which encompasses publicly funded administrative health data for the Ontario population eligible for universal health coverage (31). Preliminary results from this study confirm no improvement in statin, ACEI, and ARB prescriptions at or after guideline intervention ($p>0.05$). Statin prescription estimates were similar (62-65%) to those in the current study (52-56%) and increased rates may be attributed to the older population cohort included in ICES (age$\geq$65).

We observed better guideline adherence in urban areas and provinces including Quebec, Ontario, and the Maritimes. It is possible that dissemination outreach strategies were less effective for removed locations including rural areas and provinces such as Northwest Territories, Alberta and British Colombia. Increased distance from health care access leading to reduced frequency of physician visits may inhibit rural physicians from adhering to guidelines (32). Rural physicians report increased patient resistance to medical or preventative care as a barrier to guideline adherence (32). We also observed lower prescription rates among patients from lower SES brackets, which is consistent with low SES cohorts being less likely to receive guideline-recommended diabetes care (33).

National survey data from primary care providers across Canada highlights significant gaps in knowledge and behaviour change constructs for vascular protection (9). While awareness of the 2013 Diabetes Canada vascular protective guidelines was 71% among survey respondents, only 22% had correct knowledge of guideline content for vascular protection upon questioning, and only 21% reported adhering to guideline recommendations (9). It remains possible that despite ongoing dissemination efforts, prescription rates may have reached a ceiling in terms of any further improvements in uptake.

Limitations of this study should be acknowledged. First, the CPCSSN cohort involves a convenience sample of patients, providers, and practices, which limits the generalizability of findings. Second, results must be interpreted carefully, as prescription estimates may not correspond with actual medication usage. Third, the CPCSSN validated case definition for

diabetes differed from the 2013 Diabetes Canada guidelines definition. The CPCSSN definition includes both type 1 and type 2 diabetes, with an HbA1c ≥7% or fasting glucose ≥7 mmol/L**,** while Diabetes Canada includes an HbA1C ≥6.5% or fasting glucose ≥7 mmol/L. We suspect that CPCSSN was unable to capture some patients who would otherwise be considered as having diabetes by the Diabetes Canada guidelines, potentially overestimating the rates of statin and ACEI/ARB prescriptions, as usage of these medications is associated with higher HbA1c levels (34,35). However, we suspect that this number would have been small as patients can be captured by other diabetes criteria according to the CPCSSN case definition (14). Fourth, a lack of a validated case definition for CVD, microalbuminuria and dyslipidemia in CPCSSN may reduce the specificity and sensitivity of multiple estimates. Finally, ITS analyses cannot infer cause-effect relationships, as external factors are not accounted for. An analysis of PPIs showed similar trends as the vascular protective prescriptions under investigation, suggesting that the potential for confounding effects cannot be excluded.

There are limitations unique to using practice-based EMRs, whereby accuracy and completeness can vary across different systems, providers and sites, in turn affecting the validity of the study (36). It is possible that a full record of patient medications including those requiring manual input (non-prescription, specialist prescriptions), are not recorded in the EMR by all providers. Accordingly, data from non-prescription medications as a group are typically less accurate than prescription estimates (37). Antiplatelet agents carry significant bleeding risk, and we suspect that they would be more likely to be recorded in the EMR than other non-prescription medications with lower risk profiles. There is,also no reason to expect differences in the completeness of data pre- and post-guideline implementation.

Despite these limitations, this study captured trends in vascular protective medication prescriptions in a large sample of Canadian primary care patients with diabetes. Previous studies have primarily used provincial data, and are limited in their generalizability at a national level. Using longitudinal data enabled assessment of trends over time, and allowed for effective guideline evaluation at a population level. EMR data allowed for a more valid assessment of prescription rates, as self-reported data often overestimates medication adherence behaviour (38). EMR data also allowed us to capture the rates of non-prescription medications including antiplatelet agents, and data across greater age ranges (i.e. age <65), which are often unavailable with drug registry data.

We carried out statistical inference using an ITS design, which is considered a stronger research design than the traditional before and after longitudinal design, and remains the recommended quasi-experiment design when a randomized control trial is not feasible at the community level (39,40). The total number of patients prescribed medications per quarter were aggregated into a single population-level proportion and therefore results correspond to an intervention effect at the population level rather than the individual level. ITS has also been mainly used in conditions applicable to our study: a macro-level intervention (nation-wide guideline dissemination strategy), a uni-dimensional outcome (prescription rates for vascular protective agents), and including a large population of patients with diabetes in primary care (25).

This study highlights a persistent gap in the management of vascular protection among patients with diabetes. Qualitative assessments are needed to assess the collective experience of

physicians and elicit factors not captured in our quantitative design (i.e. registries which capture information about why a physician did not prescribe a guideline-recommended treatment). Further dissemination efforts should be targeted at groups with lower adherence rates including physicians from rural areas, and those treating patients with lower SES. They may also involve EMR-based prompts to serve as reminders for providers. It is possible that a ceiling level of vascular protective medication uptake has been achieved, however it is necessary to explore other reasons for guideline non-adherence and revise dissemination strategies accordingly before arriving at this conclusion.

ARTICLE INFORMATION

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FIGURE LEGENDS

Figure 1a. Proportion of eligible patients prescribed vascular protective medications in Canada, quarterly from 2011-2015

Diamond = statin; circle = ACEI/ARB; square = PPI (reference); triangle = antiplatelet

**Solid line indicates the intervention point of guideline publication and dissemination (2013 Q2).*

Figure 1b. Proportion of eligible patients achieving recommended LDL and BP targets in Canada, quarterly from 2011-2015

Circle = LDL; square = BP

**Solid line indicates the intervention point of guideline publication and dissemination (2013 Q2).*

Figure 2. Lag4, lead1 approach for sample quarter (2013 Q2).

**2013 Q2 represents the quarter of interest. As illustrated, data from 4 lag quarters (2012 Q2 – 2013 Q1) and 1 lead quarter (2013 Q3) will be included in the analysis for 2013 Q2.*

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Table 1. Patient, provider and geographical characteristics for statin, ACEI/ARB and antiplatelet prescriptions among patients with Type 2 diabetes

	Statin medication			ACE/ARBi medication			Antiplatelets medication		
	N	**Percent (%)**	**P-value**	**N**	**Percent (%)**	**P-value**	**N**	**Percent (%)**	**P-value**
Age (years)									
40-49	4084	56.1%	0.0006	-	-	-	814	13.4%	0.001
50-59	9766	58.6%		3023	39.8%	<.0001	2125	15.3%	
60-69	13448	58.7%		11142	48.7%		2982	15.6%	
70-79	10769	58.3%		8910	48.2%		2377	15.4%	
80+	8589	59.2%		7076	48.7%		1781	14.7%	
BMI (kg/cm^2)									
< 18.5	227	59.1%	0.33	163	51.1%	0.004	48	15.1%	0.34
18.5-24.9	4162	60.5%		2877	50.1%		902	15.8%	
25-29.9	9455	60.4%		6431	49.3%		1947	14.8%	
30-34.9	8734	59.9%		5575	47.8%		1839	15.1%	
35-39.9	4857	59.3%		2915	47.5%		987	14.4%	
>=40	3992	59.0%		2196	47.1%		821	14.6%	
Missing	15229	55.5%		9994	45.6%		3535	15.5%	
Gender									
Female	22147	58.4%	0.99	14365	47.6%	0.71	4723	14.9%	0.15
Male	24505	58.4%		15786	47.4%		5355	15.3%	
Missing	4	44.4%		.	.		1	14.3%	
SES quintiles									
1 (highest)	3958	59.4%	<.0001	2574	47.3%	0.001	847	15.2%	0.001
2	5071	61.6%		3233	49.5%		989	14.6%	
3	4577	61.1%		2919	48.4%		948	15.1%	
4	3957	58.2%		2603	48.1%		833	14.7%	
5 (lowest)	4134	56.0%		2595	45.7%		778	12.7%	
Missing	24959	57.6%		16227	47.2%		5684	15.7%	
Smoking status									
Current Smoker	4280	59.5%	<.0001	2460	48.3%	0.015	926	15.5%	0.008
Non Smoker	8065	58.0%		5356	49.0%		1614	14.0%	
Past smoker	9798	63.4%		6500	50.5%		1956	15.1%	
Missing	24513	56.6%		15835	45.8%		5583	15.4%	
Hypertension									
No	16551	50.0%	<.0001	8160	31.0%	<.0001	3481	11.7%	<.0001
Yes	30105	64.4%		21991	59.2%		6598	17.8%	
Dyslipidemia									
No	8461	41.3%	<.0001	6485	39.3%	<.0001	2240	13.2%	<.0001
Yes	38195	64.3%		23666	50.3%		7839	15.8%	
Albuminuria									
micro	11190	69.5%	<.0001	7623	60.0%	<.0001	2645	20.5%	<.0001
Normal	13861	63.2%		8438	48.7%		2898	15.4%	
macro	3372	73.1%		2493	68.2%		838	24.7%	
Missing	18233	49.0%		11597	38.9%		3698	11.7%	
CVD									

No	36395	54.6%	<.0001	23456	44.2%	<.0001	10079	15.1%	N/A
Yes	10261	77.8%		6695	64.1%				
Rurality									
rural	8895	53.9%	<.0001	5984	44.5%	<.0001	1976	14.5%	0.001
urban	33049	61.1%		21137	49.2%		7094	15.7%	
Missing	4712	50.9%		3030	42.9%		1009	12.8%	
Province									
AB	5804	45.1%	<.0001	4022	39.5%	<.0001	1076	9.9%	<.0001
BC	385	35.2%		366	41.5%		85	9.5%	
MB	9044	59.2%		5758	48.6%		1977	15.8%	
MP	1636	64.8%		1048	50.5%		540	26.3%	
NL	1941	54.0%		1421	48.6%		494	16.8%	
NW	722	56.9%		439	55.4%		200	19.2%	
ON	26194	62.4%		16483	48.9%		5519	15.6%	
QC	930	74.2%		614	55.9%		188	17.9%	
Graduation year									
1965-1979	1871	70.6%	0.15	1241	57.0%	0.18	472	20.9%	<.0001
1980-1994	5769	67.8%		3764	54.9%		1094	15.3%	
>=1995	5872	69.2%		3688	56.1%		1323	18.3%	
Non-UTOPIAN	33144	55.0%		21458	44.8%		7190	14.4%	
Total number of patients prescribed medication	**46656**	**58.4%**		**30151**	**47.5%**		**10079**	**15.1%**	
Total number of patients enrolled in dynamic cohort over study period	**79880**	**100%**		**63494**	**100%**		**66,683**	**100%**	

Table 2. Interrupted time-series regression analysis of vascular protective medication prescribing rates

		Estimate	**Standard Error**	**P value**
Statin				
	Intercept B_0	50.97	0.95	<0.0001
	Pre-intervention trend B_1	0.33	0.10	0.0072
	Level change	0.35	0.43	0.4280
	Trend change	-0.52	0.15	0.0045
ACEI/ ARB				
	Intercept B_0	41.66	0.85	<0.0001
	Pre-intervention trend B_1	0.14	0.09	0.1691
	Level change	0.37	0.45	0.4218

	Trend change	-0.38	0.13	0.0127
Antiplatelet				
	Intercept B_0	9.75	0.44	<0.0001
	Pre-intervention trend B_1	0.13	0.05	0.3918
	Level change	-0.26	0.30	0.3918
	Trend change	-0.06	0.06	0.3129
PPI				
	Intercept B_0	18.92	0.36	<0.0001
	Pre-intervention trend B_1	0.39	0.04	<0.0001
	Level change	0.31	0.21	0.1586
	Trend change	-0.18	0.05	0.0044

*Pre-intervention trend (before guideline intervention), Level change (at guideline intervention), Trend change (difference in slope before/after guideline intervention)